Original Article

Left Atrial Volume Index to Predict Long-Term Recovery of the Left Ventricular Ejection Fraction in Patients with Heart Failure and Reduced Ejection Fraction

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Abstract

Context: Left ventricular ejection fraction (LVEF) recovery is an important treatment goal for patients with heart failure (HF) and reduced EF (HFrEF); however, the applicability of the left atrial volume index (LAVI) in predicting long-term LVEF recovery in HFrEF remains unknown. **Aim:** We aimed to assess the predictive value of the LAVI in predicting long-term LVEF recovery in patients hospitalized with HFrEF. **Settings and Design:** This was a retrospective cohort study. **Materials and Methods:** We analyzed 70 decompensated patients with HF, hospitalized between 2013 and 2014, with an LVEF <40%. Patients were categorized into recovered (≥40% LVEF and ≥10% improvement in LVEF) and nonrecovered groups, according to an echocardiography-measured LVEF >3 years postdischarge. Predictive LAVI values used to predict long-term LVEF improvement were determined. **Statistical Analysis:** The survival rate was determined using Kaplan–Meier analysis. In receiver operating characteristic curve (ROC) analysis, the area under the curve (AUC) and optimal cutoff values were obtained from several echocardiographic parameters. Univariate and multivariate logistic regression analyses identified predictors of LVEF improvement. **Results:** Twenty-seven (39%) patients had recovered LVEFs. During a median follow-up period of 76 (60–80) months, the survival rate was significantly higher in the recovered group (log-rank test, $P = 0.001$). ROC analysis showed that LAVI's predictive performance in long-term LVEF improvement (AUC 0.78, 95% confidence interval [CI] 0.66–0.87) was optimal at a cutoff of 35 g/m^2. LAVI <35 ml/m^2 independently predicted LVEF improvement (odds ratio 6.02, 95% CI 1.26-28.81, p=0.025). **Conclusions:** LAVI is associated with predicting long-term LVEF improvement.

Keywords: Arrhythmia, heart failure, left atrial volume index, left ventricular ejection fraction, major adverse cardiovascular events, prognosis

Introduction

Heart failure (HF) is stratified according to the left ventricular ejection fraction (LVEF).[1] Among patients with HF and

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reduced LVEF (HFrEF), LVEF improvement is important during HF treatment.[2]

A larger left atrial diameter (LAD) has been reported to be a predictor of cardiovascular events.[3-6] Left atrium (LA) performance is not unidirectional; therefore, evaluating the size of the LA is preferable in terms of two-dimensional–based volume.[7] This study aimed to estimate the relationship between LA size, measured using the left atrial volume index (LAVI), and long-term LVEF recovery in discharged patients with HFrEF.

Materials and Methods

Study design and population

A Diagnosis Procedure Combination (DPC) database was used in the Heart Institute of Japan Heart Failure study (HIJ-HF II) retrospective, multicenter, cohort study that involved ten participating DPC hospitals in Japan. That study's design and preliminary results have been described elsewhere.[8] That study's protocol was approved by the Institutional Review Boards of Tokyo Women's Medical University. Owing to the HIJ-HF II study's retrospective design, the requirement for written informed consent was waived.

Briefly, 1245 consecutive patients hospitalized for decompensated HF across ten hospitals were enrolled in the study between April 2013 and March 2014. The diagnosis and history of HF were determined by an experienced attending cardiologist and were based on the Framingham study criteria.[9]

From the HIJ-HF II cohort, 143 decompensated HF patients with LVEFs <40% had been discharged from Tokyo Women's Medical University. Of these, 86 (40%) patients who had been followed up at Tokyo Women's Medical University and who had undergone an echocardiography examination >3 years after discharge were included in our study. Given the challenges in evaluating atrial volume measurements using echocardiography, patients with congenital heart disease, patients with implanted ventricular assist devices, and patients who had previously undergone mitral valve surgery were excluded from this study [Figure 1]. In total, our study comprised 70 patients (50 men; median age, 65 [range, 53–71] years). Echocardiography was performed 54 (range, 48–58) months after discharge to evaluate long-term recovery using LVEF data.

Data collection and endpoints

Patient background, medical history, blood test results, ultrasound data, and angiographic data were collected by a physician or a trained clinical research coordinator. The primary end point was the LVEF at the long-term follow-up examination after discharge. The secondary end point was all-cause death.

Echocardiography

We analyzed echocardiographic parameters that had been recorded for patients during their hospitalization. All

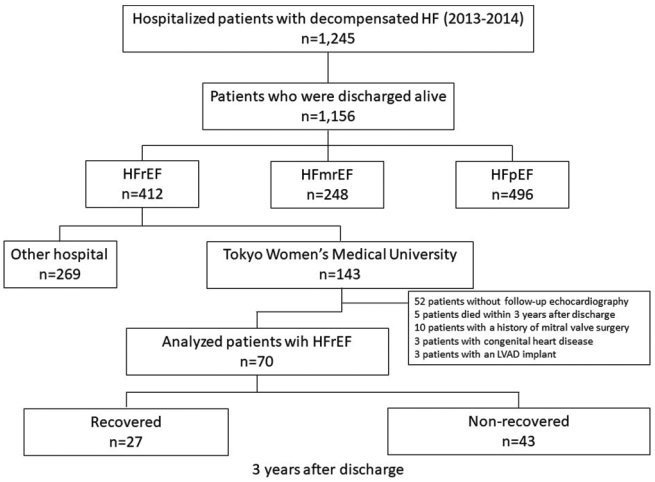

Figure 1: Flow diagram of the study patients. HF: Heart failure; HFmrEF: Heart failure with midrange ejection fraction; HFpEF: Heart failure with preserved ejection fraction; HFrEF: Heart failure with reduced ejection fraction; LVEF: Left ventricular ejection fraction; LVAD Left ventricular-assisted device

images were stored digitally, and the relevant parameters were measured according to the American Society of Echocardiography recommendations.[10] The left ventricular end-diastolic volume (LVEDV), the left ventricular end-systolic volume (LVESV), and the LVEF were calculated by the biplane-disc summation method (modified Simpson's rule), using the apical two- and four-chamber views. The LAD in end-systole was determined using the American Society of Echocardiography standards.[11] The left atrial volume (LAV) was measured using the bi-apical (two- and four-chamber views) according to the Simpson's rule at the LV end-systole.[12] The LAVI (ml/m^2) was defined as the LAV divided by the body surface area (m^2). The LV mass (LVM) was calculated as the left ventricular diastolic dysfunction (LVDd), interventricular septal thickness (IVST) at end-diastole, and posterior wall thickness (PWT) at end-diastole using the cube formula,[11] as follows:

$$LVM\ (g) = (0.8 \times 1.04) \times ([LVDd + IVST + PWT]^3 - [LVDd]^3) + 0.6.$$

The LVM index (g/m^2) was defined as the LVM (g) divided by the body surface area (m^2). The systolic velocities (slo and early diastolic velocities (elo (cm/s) were measured using tissue Doppler imaging (TDI) on the septal mitral annulus and lateral mitral annulus as a peak velocity in early diastole at the leading edge of the spectral waveform. The E-wave maximum velocity of transmitral flow was measured using pulsed-wave Doppler. Given that >30% patients with atrial fibrillation (AF) or ventricular pacing were included in this study, A-wave velocity was excluded. The E/e′ ratio was calculated using the E-wave maximum velocity and en of the septal mitral annulus.[13] The deceleration time of the E velocity was measured as the time interval from the E-wave peak to the velocity decline at baseline. The tricuspid annular plane systolic excursion (TAPSE) was measured in the apical

four-chamber view through placing the M-mode cursor optimally aligned along the direction of the tricuspid annulus. The peak excursion of the lateral annulus represented the TAPSE (mm). The right ventricular systolic pressure (RVSP) was estimated from the Doppler-derived velocity of the tricuspid regurgitation jet.[12] The color Doppler scale of mitral regurgitation (MR) was evaluated by a clinical ultrasonologist. The MR color jet area was measured on apical four-chamber, apical two-chamber, and long-axis views. To determine the severity of MR, the ratio of the MR color jet region to the LA region (MR/LA ratio) was calculated using both maximum measures. Moderate and severe MR was defined MR/LA ratios of ≥0.2 to <0.4 and ≥0.4, respectively.[14]

Statistical analysis

Continuous data are presented as numbers, and categorical data are presented as medians and interquartile ranges. The LVEF was evaluated using echocardiology >3 years after discharge and was then used to divide the patients into two groups: the recovered group, defined as an LVEF of ≥40% and ≥10% absolute improvement in LVEF, and the nonrecovered group. Continuous variables were compared using the Wilcoxon rank-sum test, and categorical variables were compared using Fisher's exact test. To evaluate the influence of the LVEF recovery with respect to subsequent death, the survival rate was analyzed using the Kaplan–Meier method. In the receiver operating characteristic curve (ROC) analysis, the area under the curve (AUC) and the optimal cutoff values for several echocardiographic parameters, including LAVI, were determined to predict LVEF improvement after discharge. Univariate and multivariate logistic regression analyses were performed to identify independent predictors of LVEF improvement among echocardiographic parameters. In the multivariate logistic regression analysis, confounding echocardiographic parameters with an AUC of >0.75 were used and further adjusted using clinical parameters identified as significant in the univariate analysis. A $P < 0.05$ was considered statistically significant. Data analyses were performed with SPSS statistical software (version 22.0, IBM Corp., Armonk, NY, USA).

Results

Patient characteristics

Data concerning 70 patients with HFrEF (median age, 64 [range, 53–71] years; males, 71%; ischemic heart disease, 31% of patients) were analyzed. The recovered LVEF group comprised 27 (39%) patients. The baseline characteristics at discharge are presented in Table 1. The recovered group had a significantly shorter QRS width at discharge than the nonrecovered group (median: 100 vs. 130 ms, respectively; $P = 0.019$). Patients in the recovered group were less likely to have ischemic heart disease than those in the nonrecovered group ($P = 0.059$). The proportion of patients who received cardiac implantable electronic devices did not differ between the two groups. Regarding medication at discharge, a greater proportion of patients in the nonrecovered group received diuretics than in the recovered group ($P = 0.002$). There were no between-group differences in terms of the administration rate of beta-blockers, angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, and mineralocorticoid receptor antagonists.

Prognosis

During a median follow-up of 76 (60–80) months, 17 (24%) patients died. The survival rate was significantly higher in patients with recovered LVEFs than in those without [5 years, 96 vs. 66%, $P = 0.001$; Figure 2].

Predictors of long-term left ventricular ejection fraction recovery

The echocardiographic characteristics before discharge are summarized in Table 2. The LV and LA were smaller in size in the recovered group than in the nonrecovered group. Baseline LVEFs were lower in the nonrecovered group. The septal e', and E/e' determined according to the TDI were also lower in the nonrecovered group. In terms of MR rates, the recovered group had a significantly lower rate of MR (moderate or severe) compared to the nonrecovered group.

Results of the univariate logistic regression analysis indicated that several echocardiographic parameters were significantly associated with LVEF recovery [Table 3]. Because some parameters were similar to each other, the following echocardiographic parameters were selected: LVEDV and LVESV as indicators of the LV size, LAVI as an indicator of the LA size, and RVSP as an index of the right ventricular pressure. The nine parameters were significantly associated with the recovered LVEF using a univariate logistic regression method [Table 3]. In the ROC curve analysis, the AUC values for the nine parameters were presented in Table 4. LVEDV, LVES, and LAVI had AUC values of >0.75. In the multivariate logistic regression analysis, which we performed using confounding parameters with AUCs >0.75 and MR that was found by to be a significant parameter by univariate analysis, LAVI <35 ml/m^2

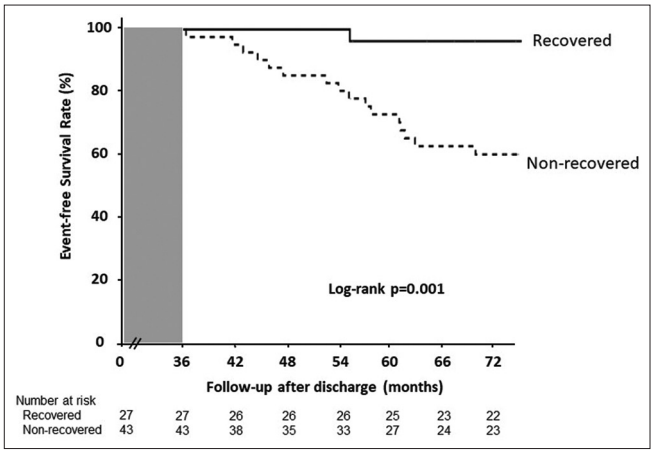

Figure 2: Kaplan–Meier's curves for all-cause death. Survival rates differed significantly between the recovered and nonrecovered left ventricular ejection fraction groups

Table 1: Patient characteristics at discharge

Variable	Overall (*n*=70)	Recovered (*n*=27)	Nonrecovered (*n*=43)	*P*
Age (years)	65 (53-71)	63 (50-70)	66 (56-72)	0.169
Male sex	50 (71)	18 (67)	32 (74)	0.487
Body mass index (kg/m^2)	24 (21-26)	21 (20-24)	24 (22-26)	0.637
Blood pressure (mmHg)	108 (98-118)	110 (106-118)	104 (96-118)	0.183
Heart rate (bpm)	70 (60-74)	70 (67-77)	68 (60-74)	0.168
NYHA Class I/II/III/IV	5/59/6/0 (7/84/9/0)	2/25/0/0 (7/93/0/0)	3/34/6/0 (7/79/14/0)	0.127
Ischemic heart disease	22 (31)	5 (19)	17 (40)	0.059
Atrial fibrillation	21 (30)	7 (26)	14 (33)	0.553
Sustained VT/VF	4 (6)	1 (4)	3 (7)	0.555
eGFR <60 mL/min/1.73 m^2	23 (33)	6 (22)	17 (40)	0.111
Plasma BNP (pg/mL)	243 (155-469)	178 (48-490)	293 (187-525)	0.255
CRT-P/CRT-D	11 (16)	4 (15)	7 (16)	0.870
ICD	3 (4)	1 (4)	2 (5)	0.848
Atrial fibrillation	9 (15)	3 (13)	6 (16)	0.687
QRS complex duration (m/s)	125 (100-160)	100 (90-160)	130 (110-160)	0.019
Medications				
ACE inhibitors/ARBs	60 (86)	25 (93)	35 (81)	0.175
Beta-blockers	63 (90)	26 (97)	37 (86)	0.138
Diuretics	51 (73)	14 (52)	37 (86)	0.002
MRAs	40 (57)	14 (52)	26 (60)	0.479
Digoxin	17 (24)	4 (15)	13 (30)	0.133

Values are presented as *n* (%) or median (IQR). IQR: Interquartile range, ACE: Angiotensin-converting enzyme, ARBs: Angiotensin II receptor blockers, BNP: brain natriuretic peptide, CRT-D: Cardiac resynchronization therapy with a defibrillator, CRT-P: Cardiac resynchronization therapy with a pacemaker, eGFR: Estimated glomerular filtration rate, ICD: Implantable cardioverter-defibrillator, MRAs: Mineralocorticoid receptor antagonists, NYHA: New York Heart Association, VF: Ventricular fibrillation, VT: Ventricular tachycardia

(odds ratio 6.02, 95% CI 1.26-28.81, p=0.025) was identified as an independent predictor of the recovered LVEF [Table 5].

Discussion

This study aimed to assess the value of transthoracic echocardiography in predicting long-term LVEF recovery among Japanese patients with decompensated HF and HFrEF. Our results, despite several limitations, showed that the LAVI was an independent predictor of long-term LVEF recovery among patients with HFrEF.

Left ventricular ejection fraction recovery

In this single-center study, 27/70 (39%) discharged patients with HFrEF had recovered LVEFs after a median follow-up period of 4.5 years. Definitions concerning LVEF improvement, background patient characteristics, number of patients, and follow-up periods have differed among previously reported studies, and the reported number of patients with HF and improved LVEFs has ranged from 10%[2] to 40%.[15] The percentage of patients with improved LVEFs (defined as LVEF <40%) in our study was 41% (29 patients), which was similar to that reported by Teeter *et al*.[15] After echocardiography at the mid-term follow-up (mean, 24 ± 7 months; range, 9–36 months), Merlo *et al*. reported that a higher proportion (37%) of patients with nonischemic cardiomyopathy showed LVEF improvement.[16] In our study, the number of patients with nonischemic heart disease was higher in patients in the nonrecovered LVEF group. Patients in the recovered group had a significantly shorter QRS width. Kimura *et al*. reported that a narrow QRS complex in patients with dilated cardiomyopathy was a predictor of improvement in cardiac function.[17] Although there was an increase in the use of medications capable of antagonizing the neurohormonal system among patients with HFrEF in our HIJ-HF[18] and CHART[19] cohorts, we considered that, based on the HF treatment guidelines,[1,20] the QRS complex on the baseline evaluation electrocardiogram could be associated with myocardial damage in patients with HFrEF.

Prognosis

Patients in the recovered group were found to have a better long-term prognosis than those in the nonrecovered group. Several studies have reported that LVEF change is an independent predictor of mortality. In a prospective study by Lupón *et al*.,[21] patients with improved LVEFs (defined as LVEF of ≥45% at 1-year follow-up) had significantly improved mortality and morbidity rates than patients with HF with a preserved ejection fraction and those with HFrEF. In a retrospective cohort study using a 40% LVEF cutoff point, Kalogeropoulos *et al*. reported that patients with improved LVEF had a lower mortality rate, less frequent hospitalizations, and fewer composite end points after 3 years.[22] Furthermore, Savarese *et al*. reported that an increased LVEF was associated with a lower risk of mortality in patients with HFrEF, whereas a decreased LVEF was associated with a higher risk of mortality.[23] However, in these previous reports, >50% of patients had ischemic heart disease, whereas only 31% of

Table 2: Echocardiographic parameters before discharge in patients

Variable	Overall (*n*=70)	Recovered (*n*=27)	Nonrecovered (*n*=43)	*P*
LVDd (mm)	62 (56-67)	56 (52-58)	65 (61-70)	<0.001
LVDs (mm)	53 (47-61)	47 (41-49)	57 (52-64)	<0.001
LVEDV (mL)	195 (149-241)	156 (124-192)	216 (181-278)	0.001
LVESV (mL)	136 (99-180)	103 (82-126)	154 (133-219)	<0.001
LVEF (%)	30 (23-34)	34 (29-36)	28 (22-31)	0.001
IVST (mm)	8 (7-10)	8 (7-10)	8 (7-10)	0.389
LVPWT (mm)	8 (8-9)	9 (8-10)	8 (7-9)	0.398
LAD (mm)	44 (38-51)	38 (35-45)	46 (42-53)	0.002
LAV (mm)	87 (61-111)	58 (46-104)	95 (72-114)	0.004
LAVI (ml/m^2)	50 (34-65)	34 (30-49)	59 (46-69)	0.001
LVMI (g/m^2)	118 (97-149)	100 (83-120)	130 (110-162)	0.001
TAPSE (mm)	15 (12-18)	15 (13-19)	15 (12-18)	0.739
Septal s' (cm/s)	3.8 (3.2-4.7)	4.2 (3.5-4.8)	3.8 (3.1-4.7)	0.319
Septal e' (cm/s)	4.5 (3.2-5.4)	5.1 (4.0-6.4)	3.7 (3.0-4.9)	0.002
Lateral s' (cm/s)	4.6 (3.9-5.4)	5.3 (4.0-6.1)	4.3 (3.8-5.0)	0.176
Lateral e' (cm/s)	5.8 (3.7-8.4)	6.7 (4.9-11.1)	5.4 (3.6-7.5)	0.067
E wave (cm/s)	70 (55-95)	66 (55-92)	76 (55-99)	0.794
E/e'	15 (13-21)	13 (11-16)	18 (15-27)	0.017
DT (msec)	158 (124-208)	160 (129-264)	156 (123-191)	0.066
TRV max (m/s)	2.5 (2.3-2.9)	2.3 (2.1-2.7)	2.6 (2.4-3.0)	0.012
RVSP (mmHg)	34 (30-44)	31 (28-40)	39 (33-52)	0.005
MR (moderate or severe)	19 (27)	3 (11)	16 (37)	0.015

Values are *n* (%) or median (IQR). IQR: Interquartile range, AR: Aortic valve regurgitation, AS: Aortic valve stenosis, DT: Deceleration time of early diastolic inflow, e': Peak early diastolic annular velocity, E/A: Ratio of peak transmitral early diastolic filling velocity to peak transmitral atrial filling velocity, E/e': Ratio of peak transmitral early diastolic filling velocity to peak early diastolic mitral annular velocity, IVST: Interventricular septum thickness, LAD: Left atrial dimension, LAV: Left atrial volume, LAVI: Left atrial volume index, LVDd: Left ventricular end-diastolic dimension, LVDs: Left ventricular end-systolic dimension, LVEDV: Left ventricular end-diastolic volume, LVEDVI: Left ventricular end-diastolic volume index, LVEF: Left ventricular ejection fraction, LVESV: Left ventricular end-systolic volume, LVESVI: Left ventricular end-systolic volume index, LVMI: Left ventricular mass index, LVPWT: Left ventricular posterior wall thickness, MR: Mitral regurgitation, N/A: Not available, RV: Right ventricular, RVSP: Right ventricular systolic pressure, s': Lowest, TAPSE: Tricuspid annular plane systolic excursion, TRV: Tricuspid regurgitant velocity

patients had ischemic heart disease in our study. Zecchin *et al*. reported that approximately 66% of patients with new-onset idiopathic dilated cardiomyopathy showed LVEF improvement 3–9 months later following optimal medical therapy, with excellent long-term prognoses during the 110 ± 63-month follow-up period.[24] Our study findings showed that long-term change in the LVEF was also associated with mortality. We defined LVEF recovery as a follow-up LVEF of ≥40% and ≥10% absolute improvement in the LVEF. These indicators in relation to the LVEF have been reported to correlate with a decrease in LV volumes.[25] It is necessary for patients with HF to undergo regular follow-ups and to have optimal treatment confirmed, including drug titration or device therapy, depending on the LVEF assessed during long-term follow-up.

Left atrial volume index and left ventricular ejection fraction recovery

In patients with congestive HF (CHF), an increased LAV typically reflects high LV filling pressure.[26] During diastole, the LA is exposed to pressure from the LV. Increased LV stiffness or noncompliance increases the LA pressure to maintain proper LV filling, and increased atrial wall tension results in atrial dilation and atrial myocardial extension.[27] Consequently, the LAV increases with the severity of diastolic dysfunction.[28,29] Sustained LV diastolic dysfunction causes stretching of cardiac myocytes, leading to LV remodeling and further neurohormonal stimulation. Therefore, the LAV is a simple noninvasive assessment of LV diastolic function.[7,26] Several studies have found that LA dilation was predictive of cardiovascular outcomes, such as AF, CHF, cardiovascular death, and stroke.[4-6] Rossi *et al*. reported that smaller baseline LAVs before cardiac resynchronization therapy (CRT) were significantly associated with LV reverse remodeling after CRT.[30] When evaluating the LA, the volumetric measurement of the LA should be preferred over the LA diameter to avoid underestimation.[31] However, the predictive value of the LAVI has not been fully evaluated in patients with HFrEF. Our study showed that the LAVI was an independent predictor of improved LVEF after discharge. Regarding the parameters related to the LV end-diastolic pressure before discharge, the E wave, E/A, and E/e' in patients with LAVIs of <35 ml/m^2 were significantly lower than those in patients with LAVIs of ≥35 ml/m^2 ('57 [37–69] vs. 82 [62–103] cm/s; 0.9 [0.7–1.3] vs. 1.7 [1.2–3.0]; and 12.8 [10.3–15.5] vs. 16.2 [13.6–24.1], respectively). In addition, DT was significantly higher in patients with larger LAVIs than in those with smaller LAVIs (208 [143–274] vs. 150 [120–183] ms, respectively). Further, LA enlargement may be associated with increased LV

end-diastolic pressure and LV diastolic dysfunction in patients with HFrEF before discharge. LA enlargement and dysfunction are common in patients with AF.[32,33] In our study, although 30% of patients had AF, the LAVI was also associated with LVEF improvement after adjustment for the prevalence of AF. MR is another related factor influencing volume overload, thus leading to LA enlargement.[34] It has also been reported that the degree of MR is associated with the LAV independent of the presence or absence of AF. A greater number of patients in the recovered group had MR; however, LAVI was independently associated with LVEF improvement by multivariate analysis.[35] Although baseline LV size and LV function were found to be important factors, as shown in the univariate logistic regression analysis (LVEDV, LVESV, and LVEF), the definition of LVEF improvement was different from that in previous studies,[21-23] the number of patients with nonischemic heart disease was high, and the sample size of this study was small. Therefore, we recommend that LAVI should be investigated during the echocardiographic evaluation of hospitalized patients with HF.

Table 3: Univariate analysis of echocardiographic parameters for predicting left ventricular ejection fraction recovery

	OR	95% CI	*P*
LVEDV (1 ml decrease)	1.02	1.01-1.04	0.001
LVESV (1 ml decrease)	1.01	1.01-1.02	0.003
LVEF (1% decrease)	1.14	1.04-1.25	0.004
IVST (1 mm increase)	1.19	0.93-1.54	0.170
LVPWT (1 mm increase)	1.25	0.90-1.76	0.185
LAVI (1 ml/m^2 decrease)	1.05	1.02-1.08	0.002
LVMI (1 g/m^2 increase)	0.98	0.96-0.99	0.006
TAPSE (1 mm decrease)	0.97	0.78-1.21	0.797
Septal s' (1 cm/s decrease)	1.26	0.77-2.06	0.348
Septal e' (1 cm/s decrease)	1.51	1.09-2.10	0.012
Lateral s' (1 cm/s decrease)	1.25	0.85-1.86	0.257
Lateral e' (1 cm/s decrease)	1.14	0.97-1.34	0.106
E wave (1 cm/s decrease)	0.99	0.97-1.01	0.375
E/e' (1 unit decrease)	0.91	0.85-0.98	0.015
DT (1 ms increase)	1.01	1.00-1.02	0.035
RVSP (1 mmHg increase)	0.92	0.86-0.97	0.005
MR (moderate or severe)	0.21	0.06-0.81	0.024

CI: Confidence interval, DT: Deceleration time of early diastolic inflow, e': Peak early diastolic annular velocity, E/e': Ratio of peak transmitral early diastolic filling velocity to peak early diastolic mitral annular velocity, IVST: Interventricular septum thickness, LAVI: Left atrial volume index, LVEDV: Left ventricular end-diastolic volume, LVEF: Left ventricular ejection fraction, LVESV: Left ventricular end-systolic volume, LVMI: Left ventricular mass index, LVPWT: Left ventricular posterior wall thickness, MR: Mitral regurgitation, OR: Odds ratio, RVSP: Right ventricular systolic pressure, s': Lowest, TAPSE: Tricuspid annular plane systolic excursion

Study limitations

This study had several limitations. First, this was a single-center, retrospective study. We could not determine the influence of treatment, including HF medications and devices at the time of echocardiography. Although echocardiography is performed routinely in our institution, selection bias may have affected the results owing to variations in the date of the follow-up echocardiography after discharge. Second, the number of study patients was very small. Because limited data were available, we excluded patients who visited other institutions after discharge. Further research is necessary to determine the mechanisms involved in the association between LVEF improvement and LAVI, and a prospective study is needed to test the prognostic importance of the LAVI in patients with HFrEF.

Conclusions

Our study findings indicated that the baseline LAVI was independently associated with LVEF recovery during long-term follow-up in patients with HFrEF. The size of the LA can be considered not only in terms of diastolic function but also as a predictor of long-term LVEF recovery among patients with HFrEF.

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Table 4: Area under the curve for relevant echocardiographic variables for left ventricular ejection fraction recovery

	AUC	Cut-off	Sensitivity (%)	Specificity (%)	Positive likelihood ratio	Negative likelihood ratio
LVEDV (mL)	0.78 (0.67-0.87)	≤201	89 (71-98)	63 (47-77)	2.4 (1.6-53.6)	0.2 (0.1-0.5)
LVESV (mL)	0.82 (0.70-0.90)	≤126	78 (58-91)	81 (67-92)	4.2 (2.2-8.1)	0.3 (0.1-0.6)
LVEF (%)	0.74 (0.62-0.84)	>32	66 (46-82)	83 (68-93)	3.8 (1.9-7.9)	0.4 (0.2-0.7)
LAVI (ml/m^2)	0.78 (0.66-0.87)	<35	60 (41-77)	93 (81-99)	8.6 (2.8-26.6)	0.4 (0.3-0.7)
LVMI (g/m^2)	0.70 (0.58-0.81)	≤107	55 (36-74)	78 (62-89)	2.5 (1.3-4.9)	0.6 (0.4-0.9)
Septal e' (cm/s)	0.68 (0.55-0.78)	>5.2	44 (26-64)	88 (74-96)	3.7 (1.5-9.2)	0.6 (0.4-0.9)
E/e'	0.73 (0.61-0.83)	≤14.6	69 (49-85)	76 (60-88)	2.8 (1.6-5.1)	0.4 (0.2-0.7)
DT (m/s)	0.62 (0.49-0.73)	>215	38 (21-58)	93 (80-99)	5.2 (1.6-17.0)	0.7 (0.5-0.9)
RVSP (mmHg)	0.72 (0.59-0.82)	≤31.2	58 (37-77)	79 (64-91)	2.8 (1.4-5.7)	0.5 (0.3-0.9)

AUC: Area under the curve, DT: Deceleration time of early diastolic inflow, e': Peak early diastolic annular velocity, E/e': Ratio of peak transmitral early diastolic filling velocity to peak early diastolic mitral annular velocity, LAVI: Left atrial volume index, LVEDV: Left ventricular end-diastolic volume, LVEF: Left ventricular ejection fraction, LVESV: Left ventricular end-systolic volume, LVMI: Left ventricular mass index, RVSP: Right ventricular systolic pressure

Table 5: Multivariate analysis of echocardiographic parameters for predicting long-term left ventricular ejection fraction recovery

	OR	95% CI	*P*
LVEDV (≤201 ml)	4.26	0.63-28.78	0.137
LVESV (≤126 ml)	3.33	0.60-18.41	0.167
LAVI (<35 ml/m^2)	6.02	1.26-28.81	0.025
MR (moderate or severe)	0.53	0.10-2.73	0.450

LAVI: Left atrial volume index, LVEDVI: Left ventricular end-diastolic volume index, LVESVI: Left ventricular end-systolic volume index, MR: Mitral regurgitation, OR: Odds ratio, CI: Confidence interval

Conflicts of interest

There are no conflicts of interest.

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